Carotid endarterectomy in octogenarians: Early results and late outcome

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Purpose: **This study was undertaken to determine the safety and efficacy of carotid endarterectomy (CEA) in the octogenarian population at the Cleveland Clinic.**
Methods: **From 1989 to 1995, 182 CEAs were performed among 167 octogenarians (98 men, 69 women) with a mean age of 83 years (median, 83 years; range, 80 to 93 years). One hundred procedures (55%) were performed for severe asymptomatic stenosis, whereas 48 (26%) were performed for hemispheric transient ischemic attacks (TIAs) or amaurosis fugax, 24 (13%) for prior stroke, and 10 (5%) for vertebrobasilar symptoms. Thirteen CEAs (7%) were combined with myocardial revascularization, and another five (3%) represented carotid reoperations. Nine arteriotomies (5%) were closed primarily, whereas the remaining 173 (95%) were repaired using either vein patch angioplasty (141, 77%) or synthetic patches (32, 18%). Two patients were lost to follow-up, but late information was available for 165 patients (180 operations) at a mean interval of 2.7 years (median, 2.4 years; maximum, 7.4 years).**
Results: **Considering all 182 procedures, there were five early (<30 days) postoperative neurologic events (2.7%), including three strokes (1.6%) and two TIAs (1.1%). An additional 15 neurologic events occurred during the late follow-up period, consisting of 11 strokes (6.1%) and four TIAs (2.2%). The Kaplan-Meier estimated 5-year rate of freedom from stroke was 85% (95% confidence interval [CI], 77% to 93%). There was one early postoperative death (0.6%) of cardiac complications 9 days after CEA. The estimated 5-year survival rate was 45% (95% CI, 33% to 57%), and the 5-year stroke-free survival rate was 42% (95% CI, 30% to 53%). Multivariable analysis yielded age at operation ($p = 0.001$), abnormal creatinine level ($p = 0.025$), and chronic obstructive pulmonary disease ($p = 0.019$) as variables that significantly influenced the survival rate. The presence of chronic obstructive pulmonary disease ($p = 0.009$) and, surprisingly, a lesser degree of contralateral internal carotid stenosis ($p = 0.003$) were found to be significantly associated with stroke after CEA. Causes of late death were cardiovascular in 16 patients (30%), unknown in 13 (24%), carcinoma in six (11%), stroke in six (11%), and miscellaneous in 13 (24%).**
Conclusions: **We conclude that CEA may be safely performed in selected octogenarians with carotid stenosis, and that the majority of these patients live the rest of their lives free from stroke. Therefore, age alone should not exclude otherwise-qualified candidates from consideration for CEA. (J Vasc Surg 1998;27:860-71.)**

Large prospective, randomized trials now have established the efficacy of carotid endarterectomy (CEA) in the prevention of ischemic stroke among both symptomatic[1,2] and asymptomatic[3] patients with severe internal carotid artery stenoses. The prevalence of stroke also is known to increase with advancing age and becomes the second leading cause of death by 85 years of age.[4] Stroke prevention among the elderly almost certainly will assume even more importance in the future because current predictions indicate that the proportion of the United States population aged 75 years or older will double from approximately 5% in 1990 to nearly 10% by 2030.[5-7]

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Despite these observations, the advisability of CEA in very elderly patients remains controversial. Although some authors have reported postoperative mortality and stroke rates after CEA in octogenarians that compare favorably with those for younger patients,[8-14] patients more than 79 years of age were excluded from randomization in both the North American Symptomatic Carotid Endarterectomy Trial (NASCET) and the Asymptomatic Carotid Atherosclerosis Study (ACAS).[3,11] Furthermore, others have suggested either that advanced age is associated with an increased mortality rate after CEA[15,16] or that CEA may not be cost-effective in patients over 75 years of age.[17]

Current limitations concerning the efficient, yet compassionate use of diminishing health care resources have generated reasonable concerns regarding the long-term benefits of CEA in octogenarians. Consequently, the present study was undertaken to determine the postoperative mortality and stroke rates associated with CEA in octogenarians at our own center, to document the late survival and stroke rates in these patients, and to identify clinical factors that may influence their ultimate outcome.

PATIENTS AND METHODS

We collected retrospective data from the hospital records of 167 consecutive patients who underwent 182 CEAs at the age of 80 years or older from January 1989 through December 1995 (Table I). Long-term information was obtained during subsequent office visits or by telephone contact with the patients, their immediate families, or their local physicians. End points were defined as death or recent follow-up within 6 months of study closure. In addition to death, outcome variables included transient ischemic attack (TIA) or stroke occurring either in the perioperative period or during late surveillance. Follow-up was complete for 165 patients, representing 180 operations. The remaining two patients were considered lost at the time of hospital discharge, each on the fourth postoperative day. The median follow-up period for the survivors was 2.2 years (mean, 2.7 years; maximum, 7.4 years).

The study group consisted of 98 men and 69 women, with a mean age of 83 years (median, 83 years; range, 80 to 93 years) at the time of their operations. One hundred nine patients (66%) had clinical evidence of coronary artery disease—defined as a convincing history of prior myocardial infarction or angina—or either Q-waves or ischemic ST-T wave changes on a 12-lead electrocardiogram. One hundred twenty-seven patients (77%) had hypertension, 22 (13%) had diabetes, 24 (15%) had a history of congestive heart failure, and 19 (12%) had chronic obstructive pulmonary disease (COPD). Only 27 patients in this age group (17%) still smoked cigarettes.

Table I. Proportion of CEAs performed on octogenarians at the Cleveland Clinic

Year	*Octogenarian operations*	*Total carotid operations*	*%*
1989	26	317	8.2
1990	14	304	4.6
1991	26	300	8.7
1992	28	342	8.2
1993	25	313	8.0
1994	25	295	8.5
1995	38	365	10.4
Total	182	2236	8.1

One hundred procedures (55%) were performed for severe asymptomatic stenosis, whereas 48 (26%) were performed for hemispheric TIAs or amaurosis fugax, 24 (13%) for prior stroke, and 10 (5%) for vertebrobasilar symptoms. One hundred thirty-seven procedures (75%) were elective, 39 (21%) were semielective, and three (2%) were emergent. The urgency of the remaining three operations (2%) could not be determined. Thirteen CEAs (7%) were combined with myocardial revascularization, and another five (3%) represented carotid reoperations. Nine arteriotomies (5%) were closed primarily, whereas the remaining 173 (95%) were repaired using either vein patch angioplasty (141, 77%) or synthetic patches (32, 18%).

The degree of preoperative internal carotid stenosis for the patients in this series was evaluated by ultrasound scan, angiogram, or both and was based on an estimation of the diameter of residual lumen compared with that of the carotid bulb. By this method, an angiographic stenosis resulting in 80% diameter reduction is equivalent to 60% stenosis by the NASCET criteria.[18] The ultrasound criteria for 80% to 99% internal carotid stenosis required both a peak systolic velocity greater than 240 cm/sec and an end diastolic velocity greater than 135 cm/sec. One hundred fifty-five procedures (85%) were performed for 80% to 99% stenosis, 20 (11%) for 60% to 79% stenosis, five (3%) for 40% to 59% stenosis, two (1%) for 20% to 39% stenosis, and none for 0% to 19% stenosis. Sixteen of the contralateral internal carotid arteries (9%) were found to be occluded, 29 (16%) had 80% to 99% stenosis, 34

Table II. CEAs performed on patients <80 years of age (Vascular Registry data; Jan. 1, 1989, to Dec. 31, 1995)

Year	*Total carotid arteries*	*Postoperative stroke*	*%*	*Postoperative death*	*%*
1989	291	10	3.4	7	2.4
1990	290	6	2.1	1	0.3
1991	273	11	4.0	4	1.5
1992	314	8	2.5	4	1.3
1993	288	3	1.0	3	1.0
1994	269	5	1.9	2	0.7
1995	328	3	0.9	2	0.6
Total	2053	46	2.2	23	1.1

(19%) had 60% to 79% stenosis, 27 (15%) had 40% to 59% stenosis, 34 (19%) had 20% to 39% stenosis, and 41 (22%) had 0% to 19% stenosis by preoperative ultrasound scan, angiogram, or both. One hundred fifty-two carotid arteries (84%) were imaged with both ultrasound and angiography, whereas 20 procedures (11%) were performed on the basis of ultrasound alone and the remaining 10 (5%) on the basis of angiography alone. For purpose of analysis, angiography results were used when available; otherwise, ultrasound data were used.

A total of 56 patients (34%) in this series had at some time undergone a myocardial revascularization procedure. Fifty-two patients (31%) underwent coronary artery bypass grafting (CABG), and four (2%) underwent transluminal coronary angioplasty. Thirteen CEAs were performed as combined procedures in conjunction with CABG, and two patients underwent staged CABG after CEA. Nine combined procedures were performed for asymptomatic 80% to 99% stenoses, whereas four were performed to correct symptomatic carotid lesions. The remaining 41 cardiac procedures were performed before the carotid operations at a median interval of 6.8 years before operation (mean, 7.3 years; range, 2 months to 22 years). Myocardial revascularization procedures were performed within 6 months of CEA in 17 patients, and within 1 year in 20; in the remaining 36 patients, it was entirely incidental.

Kaplan-Meier estimates of survival distribution[19] were generated for overall survival, freedom from stroke, and for survival from stroke or death. The association of baseline variables with the incidence of stroke and death was tested by comparing the survival curves with a log-rank test if the variable was categorical or by testing for association with a Cox proportional hazards model if the variable was continuous. A significance level of a p value of 0.05 or less was used for each hypothesis. Risk factors that influenced the rates of survival and freedom from stroke were identified by univariate and multivariable analyses for the entire series. Survival analysis using multivariable Cox proportional hazards models was used to evaluate the effects of individual variables on patient survival and freedom from stroke. Risk ratios and their 95% confidence intervals (CIs) indicate the risk of the outcome at any point in time in the risk group compared with the reference group. For continuous variables, the risk ratio compares patients with a specified increment in the variable. The c-index, an estimation of the degree of fit of the model to the actual data, was calculated for each multivariable Cox proportional hazards model.[20] SAS statistical software was used for all analyses.[21]

We chose to draw comparisons of the 5-year estimated survival rates of our study group with that of the normal U.S. population from the U.S. census data for 1991. The Census Bureau reports an abridged life table for the overall population and by gender, giving 5-year survival estimates for people 80 years of age.[22] Because men outnumbered women by a factor of 1.4 to 1 in our study, we calculated an adjusted U.S. 5-year survival rate by taking a weighted average of the U.S. estimate for men (60%) and women (72%) based on the population of men (98 ÷ 167 = 0.59) and women (69 ÷ 167 = 0.41) in our study. The overall U.S. 5-year survival rate for persons 80 years of age after gender-adjusting to fit our study is 65%.

RESULTS

Early mortality and morbidity data. Considering all 182 procedures, there were five early (<30 days) postoperative neurologic events (2.7%), including three strokes (1.6%) and two TIAs (1.1%). There was one early postoperative (<30 days) death (0.6%) from cardiac complications 9 days after CEA. Two other deaths occurred at 38 days and 50 days, respectively; one of these patients had pneumonia and congestive heart failure, whereas the other had respiratory failure and sepsis after a stroke. Both of these additional deaths were causally related to the preceding carotid operations, yielding an overall perioperative mortality rate of 1.8% (three of 167) for the entire series.

Contemporary, unpublished data from our departmental registry concerning the early postoperative mortality and stroke rates after CEA in patients 79 years of age or younger are summarized in Table II. These figures reflect postoperative in-hospital

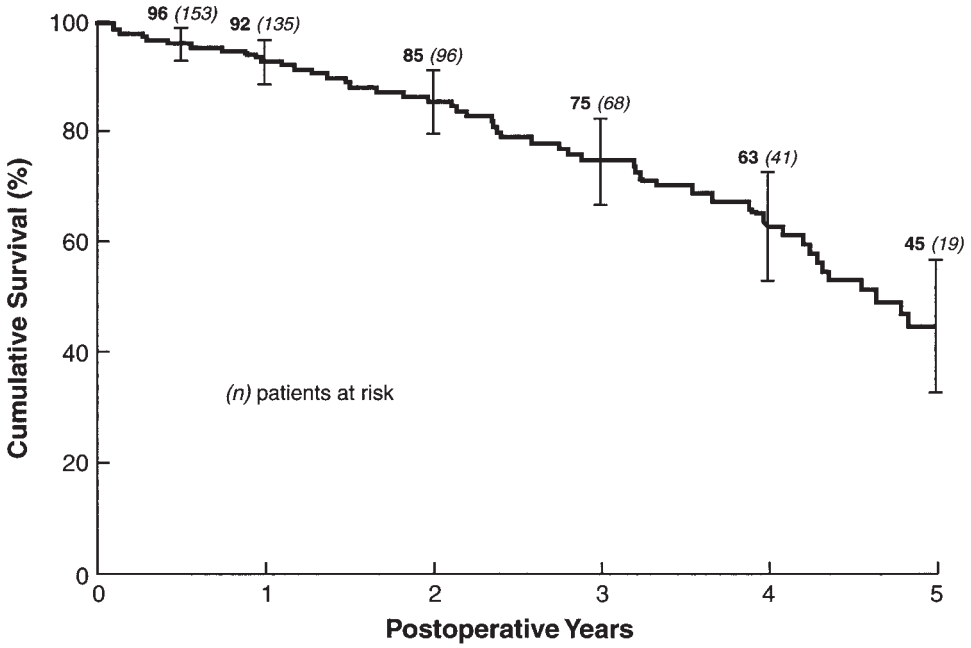

Fig. 1. Cumulative survival rate (Kaplan-Meier method) for 167 octogenarians in the entire series who underwent CEA.

(i.e., not 30-day) deaths and strokes at a time when the median postoperative length of stay was 3 days for the study interval. Nevertheless, the early postoperative stroke rate for octogenarians (1.6%) still was indistinguishable from that (2.2%) for younger patients ($p = 0.79$, Fisher's exact test). Similarly, neither the 30-day postoperative mortality rate (0.6%) nor the total perioperative mortality rate (1.8%) for octogenarians was significantly different from the hospital mortality rate (1.1%) for younger patients ($p = 0.99$ and 0.44, respectively, Fisher's exact test).

Data regarding the postoperative length of stay, defined as the interval from the date of operation to the date of hospital discharge, also are available in our departmental registry for all patients who underwent CEA from January 1990 through December 1995. The postoperative length of hospitalization for 1736 patients younger than 80 years of age (median, 3 days; mean, 5.6 days; range, 0 to 200 days) was not different from that for 155 octogenarians (median, 3 days; mean, 5.6 days; range, 0 to 55 days) who underwent CEA during the same time study period ($p = 0.09$, Wilcoxon rank-sum test).

Late survival and freedom from stroke. Late survival data for all 167 patients are illustrated in Fig. 1. The Kaplan-Meier 5-year survival rate for the entire series was 45% (95% CI, 33% to 57%) and is somewhat lower than the sex-adjusted 5-year survival rate (65%) for the normal U.S. population at the age of 80 years.[22] The probable causes for a total of 54 late deaths are summarized in Table III.

Table III. Causes of 54 late (>30 days) postoperative deaths

Cause of death	*No.*	*%*
Cardiovascular	16	30
Unknown	13	24
Carcinoma	6	11
Stroke	6	11
Renal failure	6	11
Respiratory	2	4
Miscellaneous	5	9
Gastrointestinal bleeding	1	2
Alzheimer's disease	1	2
Parkinson's disease	1	2
Ruptured aortic aneurysm	1	2
Complications of aortobifemoral bypass	1	2
Total	54	100

An additional 15 neurologic events occurred during the late follow-up period, consisting of 11 strokes (6.1%) and four TIAs (2.2%). As illustrated in Figs. 2 and 3, the Kaplan-Meier estimated 5-year rate of freedom from stroke was 85% (95% CI, 77% to 93%), and the estimated 5-year stroke-free survival rate was 42% (95% CI, 30% to 53%).

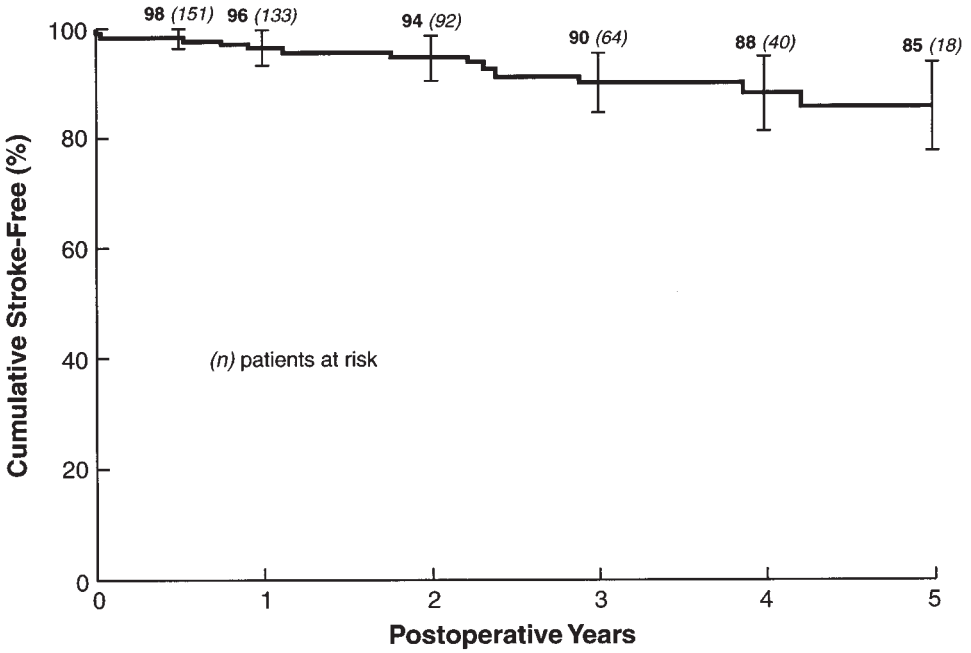

Fig. 2. Cumulative rate of freedom from stroke (Kaplan-Meier method) for 167 octogenarians in the entire series who underwent CEA.

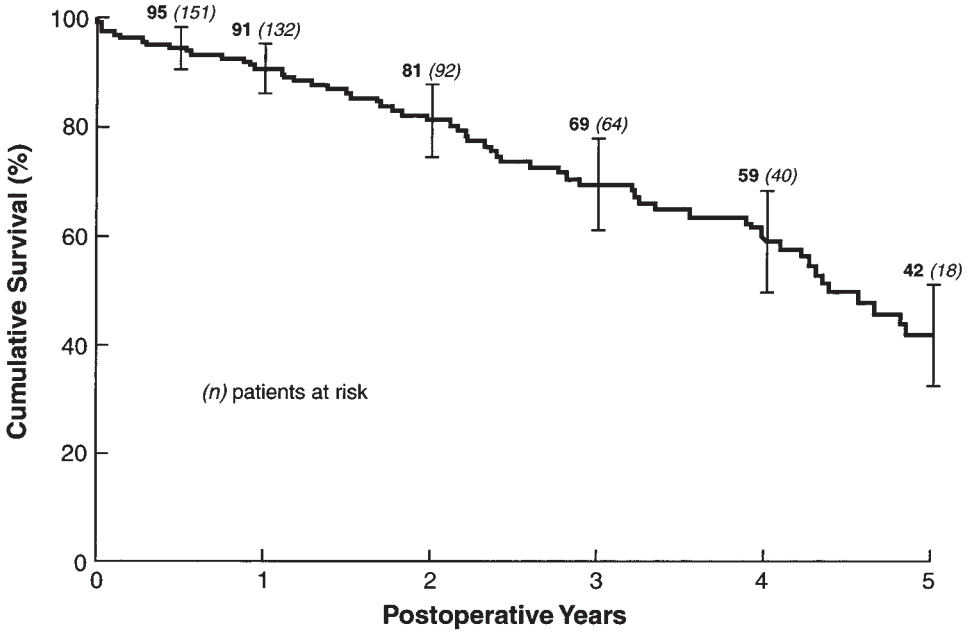

Fig. 3. Cumulative stroke-free survival rate (Kaplan-Meier method) for 167 octogenarians in the entire series who underwent CEA.

Univariate and multivariable analyses. Risk factors that potentially influenced the rates of patient survival and freedom from both early and late stroke after CEA were assessed with Cox proportional hazards models.[21] The clinical features considered and the results of these analyses are summarized in Table IV.

Through univariate analysis, we identified the presence of COPD ($p = 0.027$), and, surprisingly, a

Table IV. Univariate tests for association with stroke and survival

	Association with stroke		*Association with survival*	
Variable (risk group)	*Risk ratio (95% CI)*	*p*	*Risk ratio (95% CI)*	*p*
Gender (female)	0.79 (0.26 to 2.4)	0.67	0.70 (0.40 to 1.2)	0.20
Diabetes mellitus	0.93 (0.21 to 4.2)	0.92	0.80 (0.36 to 1.8)	0.58
Hypertension	0.81 (0.25 to 0.26)	0.72	1.2 (0.63 to 2.3)	0.57
Smoking	0.82 (0.18 to 3.7)	0.80	1.7 (0.94 to 3.2)	0.08
COPD	3.4 (1.1 to 11.0)	0.027†	2.1 (1.0 to 4.2)	0.035†
CAD	1.0 (0.33 to 3.0)	0.99	1.1 (0.62 to 1.9)	0.75
CHF	2.4 (0.75 to 7.7)	0.13	1.1 (0.57 to 2.3)	0.72
Symptoms [any of four below]	0.48 (0.16 to 1.4)	0.18	1.2 (0.68 to 2.0)	0.60
Amaurosis fugax	1.7 (0.37 to 7.4)	0.51	0.54 (0.17 to 1.7)	0.29
TIA	1.5 (0.46 to 4.7)	0.51	0.84 (0.44 to 1.6)	0.59
CVA	1.5 (0.33 to 6.7)	0.60	0.89 (0.35 to 2.2)	0.81
VBI	0.79 (0.10 to 6.1)	0.82	1.3 (0.54 to 3.0)	0.59
CABG	0.88 (0.28 to 2.8)	0.83	0.76 (0.41 to 1.4)	0.37
PTCA	3.8 (0.49 to 30.2)	0.17	1.3 (0.18 to 9.6)	0.79
Arteriotomy closure	NA	0.16	NA	0.23
Side of surgery (right)	0.86 (0.30 to 2.5)	0.77	0.70 (0.41 to 1.2)	0.19
Urgency (nonelective)	1.1 (0.29 to 3.8)	0.94	1.3 (0.69 to 2.3)	0.46
Combined CABG/CEA	0.78 (0.10 to 6.0)	0.81	0.48 (0.15 to 1.5)	0.22
Age (for 10-year difference)	5.4 (0.80 to 36.6)	0.08	5.2 (1.8 to 14.8)	0.002†
Age group (quartiles)	1.3 (0.80 to 2.1)	0.70‡	1.3 (1.0 to 1.7)	0.029
Creatinine level	0.99 (0.26 to 3.8)	0.99	2.2 (1.2 to 3.7)	0.009†
Quartiles	1.1 (0.65 to 1.8)	0.55‡	1.3 (1.0 to 1.7)	0.05
Normal vs abnormal	0.82 (0.22 to 3.0)	0.76	1.8 (1.0 to 3.1)	0.036†
Ipsilateral stenosis (for 20% difference)	0.61 (0.30 to 1.2)*	0.16	0.84 (0.49 to 1.4)*	0.52
Contralateral stenosis (for 20% difference)	0.50 (0.31 to 0.80)	0.004†	0.92 (0.78 to 1.1)*	0.36

CAD, Coronary artery disease; *CHF,* congestive heart failure; *CVA,* cerebrovascular accident; *PTCA,* percutaneous transluminal coronary angioplasty; *VBI,* vertebrobasilar insufficiency.
p value from Wald test of Cox proportional hazards model.
*Risk ratio for 20% difference in stenosis.
†$p < 0.05$; significant.
‡Test for linear trend over quartiles.

lesser degree of contralateral internal carotid stenosis ($p = 0.004$) as being significantly associated with the risk of stroke at any time after CEA. We also identified the presence of COPD ($p = 0.035$), advancing age ($p = 0.002$), and abnormal serum creatinine level ($p = 0.036$) as being significantly associated with death at any time after CEA (Table IV).

Multivariable analysis indicated the presence of COPD ($p = 0.009$) and a lesser degree of contralateral internal carotid artery stenosis ($p = 0.003$) as variables significantly associated with the risk of stroke after CEA (Table V). Multivariable analysis also yielded age at operation ($p = 0.001$), abnormal creatinine level ($p = 0.025$), and COPD ($p = 0.019$) as variables that were significantly associated with survival after CEA (Table VI). The c-index for each multivariable Cox-regression model (0.79 for the freedom from stroke model and 0.89 for the survival model, respectively) demonstrated that each fits the actual data reasonably well.[20]

In aggregate, these findings suggest that the presence of COPD, each additional year of age, and an abnormal preoperative serum creatinine level each independently and significantly is associated with the risk of dying at any time after CEA in this series. The preoperative diagnosis of COPD also was associated with an increased risk of stroke at any time after CEA. According to the Cox proportional hazards model, patients with contralateral internal carotid stenosis were less likely to have strokes over the follow-up interval, compared with those patients with a 20% decrease in stenosis. The Kaplan-Meier 3-year survival or stroke-free survival estimates for patients with and without these clinical variables are summarized in Table VII. Predicted estimates of cumulative survival for patients with COPD, abnormal creatinine level, and advancing age based on the Cox proportional hazards model derived for the patients in this series are depicted in Fig. 4. Similarly, a comparison of the predicted estimates of cumulative freedom from stroke for patients with COPD and variable degrees of contralateral internal carotid stenosis based on the Cox proportional hazards model for freedom from stroke is presented in Fig. 5.

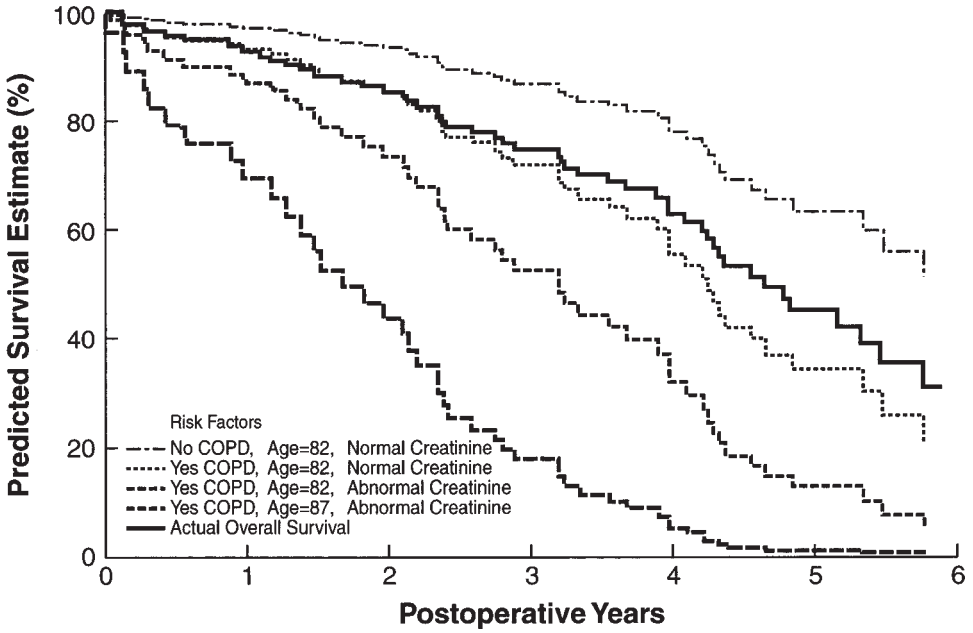

Fig. 4. Cumulative survival rate (Kaplan-Meier method) for 167 octogenarians in the entire series who underwent CEA compared with predicted estimates of cumulative survival for patients with COPD, abnormal creatinine level, and advancing age based on Cox proportional hazards model derived for patients in this series.

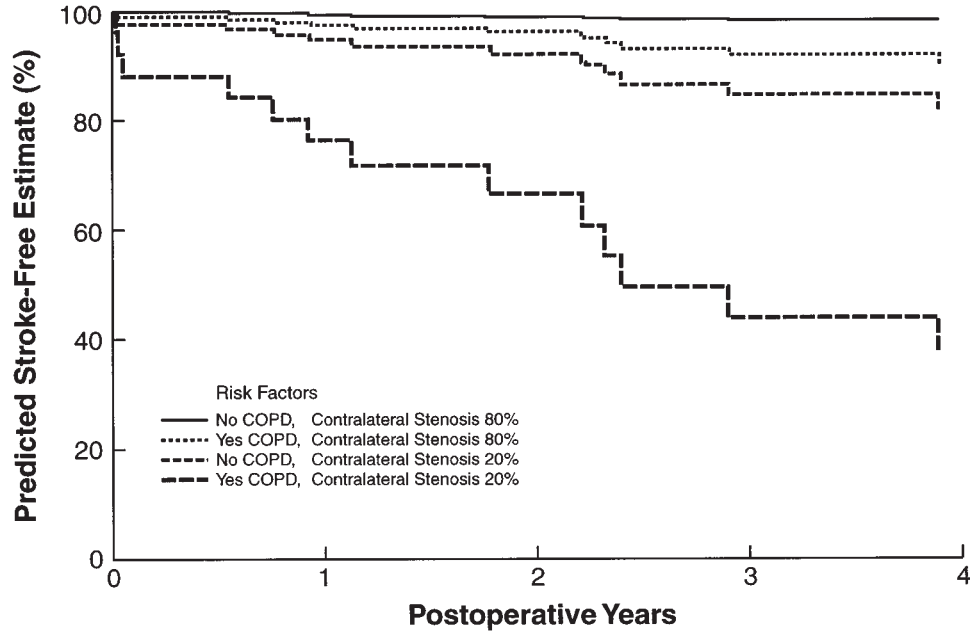

Fig. 5. Graphic representation of comparison of predicted estimates of cumulative freedom from stroke for patients with COPD and variable contralateral internal carotid stenosis based on Cox proportional hazards model derived for patients in this series.

Table V. Multivariable Cox model for association with stroke after CEA (n = 158)

	Association with stroke		
Variable	*p*	*Risk ratio reference*	*Risk ratio (95% CI)**
COPD	0.009	No COPD	4.9 (1.5 to 16.3)
Contralateral stenosis	0.003	20% difference	0.47 (0.28 to 0.77)

*Risk of stroke at any point in time in risk group versus reference. *p* value from Cox proportional hazards model, adjusting for other variables in model.

Table VI. Multivariable Cox model for association with survival after CEA (n = 155)

	Association with survival		
Variable	*p*	*Risk ratio reference*	*Risk ratio (95% CI)**
COPD	0.019	No COPD	2.3 (1.1 to 4.7)
Age	0.001	1-year increment	1.2 (1.08 to 1.37)
Creatinine (normal vs abnormal [>1.4])	0.025	Normal	1.9 (1.1 to 3.5)

*Risk of death at any point in time in risk group versus reference. *p* value from Cox proportional hazards model, adjusting for other variables in model.

Table VII, A. Cumulative survival rate associated with clinical variables among octogenarians who underwent CEA (univariate analysis)

Variable	*n*	*Cumulative 3-year survival rate (%)*	*CI (95%)*	*p*
Creatinine ≤1.4	121	78	69 to 87	0.036
Creatinine >1.4	42	65	49 to 82	
Age by quartile				0.029
Age <81 yr	43	90	79 to 100	
Age 81 to 83 yr	42	66	48 to 83	
Age 83 to 85 yr	40	78	63 to 93	
Age >85 yr	42	66	50 to 82	
No COPD	139	80	72 to 88	0.035
COPD	19	44	17 to 72	

Table VII, B. Cumulative rate of freedom from stroke associated with clinical variables among octogenarians who underwent CEA (univariate analysis)

Variable	*n*	*Cumulative 3-year stroke-free rate (%)*	*CI (95%)*	*p*
No COPD	139	92	86 to 98	0.027
COPD	19	67	38 to 97	

DISCUSSION

According to U.S. census data, life expectancy at the age of 80 years is 7.2 years for men and 9.1 years for women. By the age of 85 years, men can expect 5.3 additional years of life, and women, 6.5 years.[23] For many patients, these additional years are relatively healthy. However, stroke can be a devastating event, particularly for the very elderly, resulting in loss of function and independence.[6,24] Furthermore, the incidence of stroke is known to increase with age, and it is the second leading cause of death among patients aged 85 years or more.[4,25,26] Because of the advancing age of the population, it is likely that more elderly patients will be considered for CEA in the foreseeable future.[5-7] The economic impact of stroke on an individual is difficult to define with precision because of the many variables involved, but it is intuitively clear that strokes are very expensive.[17]

The octogenarians in our series had severe carotid occlusive disease. Nearly all (96%) of the internal carotid arteries operated on had at least 60% to 79% stenosis documented by duplex ultrasound or angiography, and 84% had ≥80% stenosis. Nearly half were symptomatic, usually despite antithrombotic therapy. Based on an annual stroke risk of 2% to 7% for asymptomatic internal carotid stenoses[3,17] and 13% for symptomatic lesions,[1] the annual risk of stroke among the octogenarians in this series could conservatively be estimated to be at least 10% without surgical intervention.

The 30-day operative mortality rate for octoge-

narians who underwent CEA was 0.6% in our series. However, the true operative mortality rate is more realistically 1.8% because two additional deaths, at 38 and 50 days after operation, were clearly related to CEA. Nevertheless, the operative mortality rate for octogenarians did not significantly differ from that for younger patients who underwent CEA, an observation reported elsewhere.[10,11,27] Although others have reported longer postoperative hospitalization intervals after CEA in the very elderly,[11] we were not able to demonstrate any difference in the postoperative acute care hospitalization requirements between octogenarians and younger patients in our series. Furthermore, the 30-day postoperative stroke rate for octogenarians in our series (1.6%) also was indistinguishable from the in-hospital stroke rate for younger patients (2.2%), whose median postoperative length of stay was 3 days during the same study period. These observations support the conclusion that the early results of CEA are as good for properly selected octogenarians as they are for younger patients.

Although the median age of the octogenarians in our series was 83 years, their cumulative 5-year survival rate after CEA (45%) compares reasonably well with the sex-adjusted 5-year survival rate (65%) estimated for the normal U.S. population at the age of 80 years, a full 3 years younger. Furthermore, their 5-year rate of freedom from stroke was 85%, indicating that most of these patients lived the rest of their lives without strokes. In fact, nearly half (42%) of our patients lived an additional 5 stroke-free years despite a median age of 83 years at the time of their CEAs. The relationship of the late strokes to carotid bifurcation disease remains uncertain because the hemispheric distribution of all of the late strokes could not be accurately determined. Moreover, the observation that six late deaths (11%) were caused by strokes underscores the fact that CEA cannot prevent all late strokes, because some undoubtedly are caused by other factors, such as cardiac arrhythmias or hypertension. Finally, the causes of 13 late deaths (24%) were undetermined, and therefore it is possible that some were stroke-related. Nevertheless, these results, in a group of octogenarians conservatively estimated to have an annual stroke risk of 10%, support the efficacy of CEA in preventing late strokes in selected surgical candidates.

In an attempt to develop guidelines for the selection of octogenarians who are likely to derive long-term benefit from CEA, clinical variables associated with rates of patient survival and freedom from stroke were investigated using univariate and multivariable analysis. The preoperative clinical diagnosis of COPD, an abnormal preoperative serum creatinine level, and advancing age each emerged as significant independent variables associated with declining late survival. To graphically demonstrate the independent influence of these clinical factors, predicted estimates of late survival after CEA for four clinical scenarios were generated with a Cox proportional hazards model (Fig. 4). For comparison, the observed survival data also are displayed and indicate that most of the patients selected for CEA were close to 80 years of age and had normal renal and pulmonary function. To validate this model, additional patients would need to be studied prospectively to determine how well the predicted data fit the observed results. Nonetheless, this model can function as a useful complement to clinical judgement.

The relationship of the clinical variables that emerged from the univariate and multivariable analysis as significant independent predictors of stroke is less clear. Patients with the clinical diagnosis of COPD were found to be 4.9 times more likely to have a stroke at any time after CEA than those without COPD. Even more surprising is the observation that patients with a 20% increase in contralateral internal carotid stenosis with respect to the comparison group had 47% less risk of stroke at any time after CEA. This conclusion seems counterintuitive and may represent an artifact of this series of patients, or it may merely reflect how few strokes occurred. Alternatively, it may reflect compensation by collateral flow. Other investigators have reported that stenosis of the contralateral internal carotid artery was not associated with increased early postoperative stroke risk at the time of CEA.[28,29] A comparison of the predicted estimates of cumulative freedom from stroke for patients with COPD and variable contralateral internal carotid stenoses based on the Cox proportional hazards model derived for the patients in this series is shown in Fig. 5. Speculation aside, a prospective validation of the model would be required to confirm the clinical relevance of these predictions.

CONCLUSION

Elderly patients with severe carotid disease tolerate CEA with excellent early and late results. Early postoperative mortality rate, stroke risk, and postoperative length of hospital stay are indistinguishable from younger patients in our experience. Late survival is favorably associated with a low preoperative creatinine level, the absence of COPD, and a lower

age. An increasing severity of contralateral carotid stenosis probably does not increase the risk for early or late stroke in this series. Late freedom from stroke is unfavorably influenced by the presence of COPD.

We conclude that CEA is safe and clearly beneficial in selected octogenarians with severe and/or symptomatic internal carotid stenosis, and that the majority of these patients live the rest of their lives free from stroke. Repair of serious carotid occlusive disease sufficiently enhances the long-term stroke-free survival rate in octogenarians that age alone should not be considered arbitrarily as a surgical contraindication without further objective investigation. Although recommendations regarding which elderly patients should or should not undergo CEA should be individualized, our data suggest that younger octogenarians with adequate pulmonary and renal function are good, not poor, candidates for CEA.

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DISCUSSION

Dr. Joseph R. Schneider (Evanston, Ill.). Dr. O'Hara and his colleagues have presented the Cleveland Clinic results for what is probably the largest, at least the largest reported, series of octogenarians who underwent carotid endarterectomy. This sample size provides good statistical power and confidence in the reliability of their data. Their early results were excellent, with a 1.6% perioperative stroke rate and a 1.8% perioperative mortality rate, despite the fact that several operations were reoperations, emergencies, or combined carotid endarterectomy and coronary artery bypass graft efforts. The late results present some fascinating questions.

When one considers the fact that 55% of their operations were performed on asymptomatic patients, the assessment of the 5-year stroke-free estimate of 85% becomes a little more difficult. As we know, the 5-year stroke-free estimate was 89% in the medically treated patients, which was virtually indistinguishable from the rate for all patients in the present study. However, the stroke-free estimates were substantially lower. That is, more strokes occurred in the medical arms of the North American Symptomatic Carotid Endarterectomy Trial than in the European Carotid Surgery symptomatic trial. For example, the 2-year stroke-free rate was estimated at 74% compared with the 70% to 99% stenosis stratum in the medical arm of North American Symptomatic Carotid Endarterectomy Trial. These trials excluded octogenarians and symptomatic older patients who possibly would have a different risk of stroke from younger patients when treated medically. Furthermore, Dr. O'Hara's manuscript did not state whether all the strokes observed were in the hemisphere ipsilateral to an endarterectomy in an octogenarian. Therefore, my first question asks whether all your postoperative strokes were ipsilateral to an endarterectomy? Second, did you find that patients who were symptomatic were distinguishable from patients who were asymptomatic with respect to late freedom from stroke? My third question asks how the distribution of symptomatic versus asymptomatic in your octogenarians, which was 45% to 55%, compares with that distribution in the Cleveland Clinic's patients who were younger than 80 years? I was intrigued to find that chronic obstructive pulmonary disease was a highly significant predictor of mortality rate despite the fact that pulmonary failure was not listed as a cause of death for any of the patients who were known to have died. I was even more surprised and intrigued to see chronic obstructive pulmonary disease as a predictor of stroke. My fourth question asks you to comment on a possible mechanism to explain why chronic obstructive pulmonary disease should be associated with stroke. Fifth and finally, given a 4.9-fold higher risk of stroke and a 2.3-fold higher risk of stroke in your study, should one consider advanced chronic obstructive pulmonary disease a contraindication to carotid endarterectomy in octogenarians? Despite concerns about the declining value of carotid endarterectomy as age increases, we too have performed carotid endarterectomy in otherwise vigorous patients as old as 93 years with no perioperative deaths and gratifying early and late freedom from stroke in the octogenarian group.

No clinical study can provide a simple answer for every patient we evaluate, and I believe clinical judgement will continue to dominate decision-making once the appropriate stenosis thresholds have been reached. Furthermore, low perioperative morbidity rates and mortality rates are essential if real benefit is to be derived from carotid endarterectomy, most especially for asymptomatic patients. Institutions and surgeons with Dr. O'Hara's exemplary results can justify a recommendation for carotid endarterectomy and selected octogenarians and even nonagenarians. I am grateful to Dr. O'Hara and to the society for the opportunity to review and comment on this well-analyzed study and well-written paper, and I commend all of you.

Dr. Patrick J. O'Hara. Dr. Schneider, I appreciate your kind comments and your questions, and I will answer them in order. The first question asked whether all of our strokes were ipsilateral to the endarterectomy, and the answer is that unfortunately we were not able to determine, for all of the patients, the hemisphere involved because of the nature of the study. So, the answer is that this study encompasses all strokes, and we do not know really whether they are all ipsilateral or contralateral. This is a shortcoming of this study. Do you find that symptomatic patients were indistinguishable from asymptomatic patients with respect to late freedom of stroke? We were unable to distinguish between symptoms versus no symptoms because the difference was not significant. How is the distribution of symptomatic versus asymptomatic patients compared with general practice? I do not have the figures for our general practice, but my impression is that the distribution is generally the same. We perform a fair number of carotid endarterectomies in asymptomatic patients who have 80% to 99% stenosis, very tight carotid lesions, because we believe the operation is beneficial in general and for the octogenarian. So I would say the distribution is about the same. As to the question regarding the possible mechanism to explain why chronic obstructive pulmonary disease is associated with stroke, it is fascinating. The short answer is that no, we do not know what the mechanism is. The multivariable analysis shows that chronic obstructive pulmonary disease is associated with a higher risk of stroke, but we cannot imply cause and effect. It may be that what we were measuring as chronic obstructive pulmonary disease is actually related to another variable that may influence the stroke rate, so they may not be linked directly. Thus the short answer is that we do not know, but certainly we should look into it further. You asked, in the last question, whether chronic obstructive pulmonary disease would be a contraindication to endarterectomy,

given a five-times higher risk of stroke and a higher risk of death in this study associated with chronic obstructive pulmonary disease. I suppose it would be a relative contraindication. We tried to show this influence by the proportional hazards model that was one of the last slides. It should factor in as a complement to clinical judgement, but there is obviously still room for clinical judgement. I would like to thank you for the questions.